UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,366	09/19/2003	Fen Huang	34506.143	8954

25005 7590 03/07/2007

DEWITT ROSS & STEVENS S.C.
8000 EXCELSIOR DR
SUITE 401
MADISON, WI 53717-1914

EXAMINER	
HUTSON, RICHARD G	
ART UNIT	**PAPER NUMBER**
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,366	HUANG ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendment of claims 1, 5, 10, 14, 18, 22, 26, 31, 33, 37, and 42 and specification, in the papers of 11/30/2006 and 12/11/2006, are acknowledged. Applicants' arguments filed on 11/30/2006, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Claims 1-45 are still at issue and are present for examination. Claims 1-45 are still at issue and are present for examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was stated in the previous office action as it applied to previous claims 1-45. In response to the rejection applicants have amended claims 1, 5, 10, 14, 18, 22, 26, 31, 33, 37, and 42 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse the rejection on a number of different basis. First applicants submit that statements made in the previous office action were overly broad and did not consider the series of verbs contained in each of the independent claims. Applicants point is so noted and while it is believed that such an interpretation was previously made, it was done so only so that the issues upon which the rejection was based could be focused on rather then the "series of verbs" used in the claims. Applicants point is acknowledged and as such the examiner will try to focus not only on the issues upon which the rejection is based, but also on the series of verbs used in each of the different independent claims.

Secondly applicants submission that the claims to not recite any and all "RNase inhibitors", but rather any and all "RNase inhibitor proteins" is also acknowledged.

Applicants thus submit that the office is ascribing an unreasonably broad interpretation to the scope of the claims.

With respect to nature of the "RNase inhibitor protein", applicants submit that contrary to the office's assertion that "the specification only uses heat and either rat or human RNasin...", applicants submit that the specification contains a detailed description, including prior art reference citations of human, pig and rat RNase inhibitor proteins. Applicants submit that a host of different RNase inhibitor proteins are known in the art, as these can be commercially purchased from several companies.

Applicants submit that the class of inhibitor proteins recited in the claims do share an important structural characteristic, i.e. 1) that they be proteins and 2) capable of inhibiting RNase. Applicants further submit a patent application is not aimed at a

casual reader, but rather a person of ordinary skill in the art and based upon this level of knowledge, one of skill in the art would be perfectly capable of determining whether or not a protein is capable of inhibiting RNase. Applicants submit that the subject matter in the claims does not need to be described literally in the specification. Applicants submit that the listing of a number of exemplary species that fall with in a generic term is perfectly valid and approved approach to defining such a generic term.

Thus applicants conclude by submitting that the present specification's teachings of the human, rat and porcine-derived RNase inhibitor proteins in combination with known commercially available proteins, clearly conveys to a person of ordinary skill in the art that applicants were in possession of the invention at the time the application was filed.

Applicant's complete argument is acknowledged and has been carefully considered, however, is found nonpersuasive for the reasons previously made of record and repeated herein. Applicants assertion that the shared important structural feature of the referenced RNase inhibitor proteins is that they are proteins is not a convincing argument. As pointed out each of the referenced RNase inhibitors must be a protein, however, this remains an incredibly broad structural genus with respect to the claimed function of RNase inhibition, and even more so when the claimed proteins must maintain this RNase inhibition function in the presence of and thereafter at least 50°C heat. Further applicants are reminded that in addition to the above functions, such a claimed combination must achieve that "RNA present in the mixture or subsequently added to the mixture is protected from enzymatic degradation by Rnases".

As previously stated, the specification also fails to describe additional representative species of RNAase inhibitor proteins for use in the claimed methods by any identifying structural characteristics or properties necessary to ensure the successful use of these inhibitor proteins, i.e. the combination of the RNase inhibitor protein and the specifically recited temperature conditions. Given this lack of additional representative species as encompassed by the claims, and lack of structural to functional characterization, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 5, 14, 22, 31, , 37 and 42 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 5, 14, 22, 31, , 37 and 42 are further rejected under this statue because the newly added recitation to "recombinant sources of human placental proteins" is not supported by the specification at the time of original filing and is thus considered new matter.

Previously applicants rejected claims recited that the RNase inhibitor protein is derived from a "recombinant human placental source" while the newly amended claims recite that the RNase inhibitor protein is derived from a "recombinant source of human placental proteins. Clearly the scope of the newly amended claims is different than that which was previously claimed. Without support for such a source of RNase inhibitor proteins, this newly added recitation is considered new matter.

Claims 1-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed methods of use of rat or human RNAsin, does not reasonably provide enablement for the claimed methods of use of any RNAase inhibitor protein in combination with the specified temperature and having the specified results. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was stated in the previous office action as it applied to previous claims 1-45. In response to the rejection applicants have amended claims 1, 5, 10, 14, 18, 22, 26, 31, 33, 37, and 42 and traverse the rejection as it applies to the newly amended claims.

As above applicants traverse the rejection on a number of different basis. First applicants submit that statements made in the previous office action were overly broad and did not consider the series of verbs contained in each of the independent claims.

Applicants point is so noted and while it is believed that such an interpretation was previously made, it was done so only so that the issues upon which the rejection was based could be focused on rather then the "series of verbs" used in the claims. Applicants point is acknowledged and as such the examiner will try to focus not only on the issues upon which the rejection is based, but also on the series of verbs used in each of the different independent claims.

Applicants submit that the previous rather lengthy discussion of structure/function relationships, knowledge and guidance of which amino acids in the protein's sequence are critical to the desired function is irrelevant to the issue of enablement, as the person of ordinary skill in the art need only buy a commercially available RNase inhibitor, as knowledge of how an invention functions is irrelevant.

With respect to the nature of the "RNase inhibitor protein", applicants submit that the specification contains a detailed description, including prior art reference citations of human, pig and rat RNase inhibitor proteins. Applicants submit that a host of different RNase inhibitor proteins are known in the art, as these can be commercially purchased from several companies.

Applicants continue to submit a patent application is not aimed at a casual reader, but rather a person of ordinary skill in the art and based upon this level of knowledge, one of skill in the art would be perfectly capable of determining whether or not a protein is capable of inhibiting RNase. Applicants submit that the subject matter in the claims does not need to be described literally in the specification. Applicants submit

that the listing of a number of exemplary species that fall with in a generic term is perfectly valid and approved approach to defining such a generic term.

Thus applicants conclude that the present specification's teachings of the human, rat and porcine-derived RNase inhibitor proteins in combination with known commercially available proteins, clearly conveys to a person of ordinary skill in the art the knowledge, to practice the invention at the time the application was filed, using only at the most routine experimentation.

Applicant's complete argument is acknowledged and has been carefully considered, however, is found nonpersuasive, for the reasons previously made of record and repeated herein. Applicants assertion that the shared important structural feature of the referenced RNase inhibitor proteins is that they are proteins is not a convincing argument. As pointed out each of the referenced RNase inhibitors must be a protein, however, this remains an incredibly broad structural genus with respect to the claimed function of RNase inhibition, and even more so when the claimed proteins must maintain this RNase inhibition function in the presence of and thereafter a temperature of at least 50°C. Further applicants are again reminded as above, that in addition to the above functions, such a claimed combination must achieve that "RNA present in the mixture or subsequently added to the mixture is protected from enzymatic degradation by Rnases".

Applicants argument is not fond persuasive because while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants

(i.e., encoding a Rnae inhibitor protein) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without effecting the desired activity(i.e. RNase inhibitor activity in the presence of and thereafter a temperature of 50°C); (B) the general tolerance of any RNAse inhibitor protein to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of any RNAase inhibitor protein with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the necessary activity for the claimed methods and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not, it would require undue experimentation for one skilled in the art

to arrive at the majority of those methods of the claimed genus having the desired result.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including those methods of use of any RNase inhibitor protein of variant thereof in combination with a temperature of at least 50°C. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 7-9, 18-22 and 24-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Ambion, Inc. (TechNotes 8(2), SUPERase.In: The Right Choice for Protecting your RNA, web page, www.ambion.com/techlibb/tn/82/823.htm, March 2001, see IDS).

Ambion, Inc. teach a method comprising to a fist solution adding a second solution containing an amount of an RNase3 inhibitor protein (i.e. SUPERase.In) in a buffer devoid of reducing agents to yield a mixture and heating the mixture to a temperature of 67°C for 15 minutes (See figure 2 and supporting text). The RNase inhibitor SUPERnasin is derived from a mammalian source. And thus the methods taught by Ambion, Inc. anticipate claims 1-5, 7-9, 18-22 and 24-25.

Conclusion

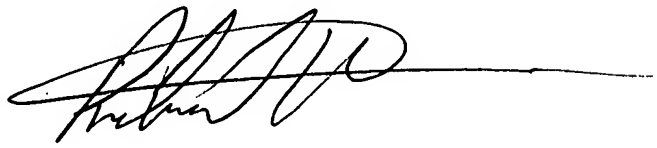
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
2/8/2007